microscope, the plaques, which have a property of sticking to the glass slip, will be found to fill the field; some will be isolated, some will be in groups; they will now appear glistening and granular, and their contours are jagged, becoming more and more so as time elapses; finally only a granular mass will be found. If, however, a drop of osmic acid be placed on the finger before the drop of blood be drawn, all the elements will be found presenting their normal appearances, and the plaques will be seen as pale homogeneous structures varying greatly in size, but for the most part about one-third or one-fourth of the diameter of the red corpuscles; they are biconcave, but not as much so as the red corpuscles. Once thus hardened they never change their form, but the plaques first referred to will be found to alter their form very speedily, and *pari passu* with these changes, processes are seen which run out from the granular masses, and when coagulation sets in these processes are nearly always found to be continuous with threads of fibrin. The connection between the breaking down of the blood is not histological but chemical. The plaques appear to give up a soluble substance which is active in coagulation. This active agent is most probably a *fibrin* ferment. Fibrin is deposited histologically independent of any of the cellular elements of the blood, and when the clot is very scant. The fibrin is seen deposited as long, needle-shaped, crystal-like bodies. — *Studies from Biolog. Lab., Johns Hopkins Univ.*, vol. iii. No. 6, May 1886.

ON RECENT PROGRESS IN THE COAL-TAR INDUSTRY[1]

II.

AZO-COLOURS.—Amongst the most important of the artificial colouring matters may be classed the so-called azo-colours. These colours are chiefly bright scarlets, oranges, reds, and yellows, with a few blues and violets. They owe their existence to the discovery by Griess, in 1860, of the fact that the so-called azo-group $-N=N-$ can replace hydrogen in phenols and amido-compounds. But it is to Dr. O. N. Witt that is due the honour of having given the first start in a practical direction to the chrysoidine class of azo-colours by the discovery of chrysoidine, and perhaps still more so by the suggestions contained in a paper read before the Chemical Society. Dr. Caro, of Mannheim, was also acquainted with several compounds which belong to this class at the time Witt published his results, but it does not appear that he made practical use of them until Witt introduced the chrysoidines and tropeolines. To Roussin, of the firm of Poirrier of Paris, is due the credit of having first brought into the market some of the beautiful azo-derivatives of naphthol. Griess, therefore, as the original discoverer of the typical compounds and reactions by which the azo-colours are obtained, may be considered as the grandfather, whilst Roussin and Witt are really the fathers, of the azo-colour industry. Nor must it be forgotten that it is to Perkin we owe the recognition of the value of the sulpho group in relation to azo-colours, a discovery patented in 1863. Moreover it is interesting to note that changes in colour from yellow to red and claret are effected by the increase in the molecular weights of the radicals introduced as well as by the relative positions occupied by these groups.

Indophenol.—Witt is also the discover of a new blue dye-stuff termed indophenol, which has been used as a substitute for indigo. Certain difficulties, however, have arisen in the adoption of this colour on the large scale. The most important use indophenol is at present put to is for producing dark blues on reds dyed with azo-colours, both on wool and cotton. The piece goods are dyed a uniform red first, and then printed with indophenol white; for like indigo itself indophenol yields a colourless body on reduction, and this being a very powerful reducing agent destroys the azo-colour, being itself transformed into indophenol blue. The process works with surprising nicety and is very cheap. The blue is formed and the red discharged with such precision that patterns can be produced in which the blue discharge covers a great deal more space than the original red. This new printing process was devised by Mr. H. Koechlin, of Lorrach. The reds used for the purpose are in the case of wool the usual azo-scarlets, for cotton Congo red.

Artificial Indigo.—About five years ago the speaker had the honour of bringing before this audience[1] the remarkable discovery made by Baeyer of the artificial production from coal-tar products of indigo blue. Since that time but little progress has been made in this manufacture, as the cost of the process, unlike the case of alizarin, has as yet proved too serious to enable the artificial to compete successfully in the market with the natural indigo.

Through the kindness of a number of eminent colour manufacturers in this country and on the Continent, the speaker was enabled to illustrate his subject by a most complete series of specimens both of the colours themselves and of their application to the dyeing and printing of fabrics of all kinds. His thanks are especially due to his friend, Mr. Ivan Levinstein, of Manchester, for the interesting series of samples of cloth dyed with known quantities of fifty different coal-tar colours, each having a different chemical composition; also to the same gentleman, and to Messrs. Burt, Boulton, and Haywood, of London, for the interesting and unique series of specimens indicating the absolute quantities of products obtainable from *one ton of coal*, as well as for much assistance on the part of Mr. Levinstein in the preparation of the experimental illustrations for this discourse. To Dr. Martius of Berlin for a valuable series of colours, especially the well-known Congo red, made by his firm, including samples of wool dyed therewith, he is also much indebted. For the interesting details concerning indophenol and its applications the speaker owes his thanks to Dr. Witt and M. Koechlin.

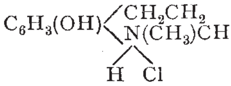
Coal-tar Antipyretic Medicines.—Next in importance to the colour industry comes the still more novel discovery of the synthetical production of antipyretic medicines.

Up to this time quinine has held undisputed sway as a febrifuge and antiperiodic, but the artificial production of this substance has as yet eluded the grasp of the chemist. Three coal-tar products have, however, been recently prepared which have been found to possess strong febrifuge qualities, which if still in some respects inferior to the natural alkaloids, yet possess most valuable qualities, and are now manufactured in Germany at Höchst and at Ludwigshafen in large quantity. And here it is well to call to mind that the first tar colouring-matter discovered by Perkin (mauve) was obtained in 1856 during the prosecution of a research which had for its object the artificial production of quinine.

In considering the historical development of this portion of his subject, the speaker added that it is interesting to remember that the initiative in the production of artificial febrifuges was given by Prof. Dewar's discovery in 1881 that quinoline, the basis of these antipyretic medicines, is an aromatic compound, as from it he obtained aniline. Moreover that Dewar and McKendrick were the first to observe that certain pyridine salts act as febrifuges. So that these gentlemen may be said to be the fathers of the antipyretic medicines, as Witt and Roussin are of the azo-colour industry.

Kairine, the first of these, was discovered by Prof. O. Fischer, of Munich, in the year 1881, whilst engaged on his investigations of the oxyquinolines. The febrifuge properties of this substance were first noticed by Prof. Filehne, of Erlangen. Kairine is manufactured from quinoline, a basic product derived from aniline by heating it with glycerin and nitrobenzene by the following process. When treated with sulphuric acid, SO_4H_2, it forms quinoline sulphonic acid, and this when fused with caustic soda yields *oxyquinoline*, which is then reduced by tin and hydrochloric acid into tetrahydroxyquinoline, and this again on treatment with C_2H_5Br yields ethyl-tetraoxyquinoline or kairine. The lowering of the temperature of the body by this compound is most remarkable, though, unfortunately, the action is of much shorter duration than that effected by quinine itself; but on the other hand, with the exception of its burning taste, it exerts no evil effects such as are often observed after administration of large doses of quinine. The commercial article is the hydrochloride, the price is 85*s.* per lb., and the quantity manufactured has lately diminished owing to the discovery of the second artificial febrifuge, antipyrine.

The following graphical formula shows the constitution of kairine:—



$$C_6H_3(OH)\begin{cases} CH_2CH_2 \\ N(CH_3)CH_2 \\ \;\;H\;\;Cl \end{cases}$$

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[1] A Discourse by Prof. Sir Henry E. Roscoe, M.P., LL.D., F.R.S., delivered at the Royal Institution, Friday, April 16, 1886. Continued from p. 114.

[1] "On Indigo and its Artificial Production," *Proc. Roy. Inst.*, May 27, 1881.

Antipyrine, the second of these febrifuges, was discovered in 1883 by Dr. L. Knorr in Erlangen, and its physiological properties were investigated by Prof. Filehne, of Erlangen. The materials used in the manufacture of antipyrine are aniline and aceto-acetic ether. The aniline is first converted into phenylhydrazine, a body discovered by Emil Fischer in 1876. This body combines directly with aceto-acetic ether, with separation of water and alcohol, to form a body called pyrazol ($C_{10}H_{10}N_2O$). The methyl derivative of pyrazol derived by treating it with iodide of methyl, is *antipyrine*, its composition being $C_{11}H_{12}N_2O$. As a febrifuge, antipyrine is superior in many respects to kairine and even to quinine itself. It equals kairine in the certainty of its action, whilst in its duration it resembles quinine. It is almost tasteless and odourless, is easily soluble in cold water, and takes the form of a white crystalline powder. Its use as a medicine is accompanied by no drawbacks. It occurs in commerce in the free state. The production of antipyrine, in spite of these valuable qualities, is as yet small, its chief employment being in Germany, where it has been successfully used in cases of typhoid epidemic. The price is 6*s*. per pound.

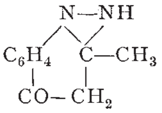
The following equations explain the formation and constitution of this interesting body. The foregoing febrifuges are manufactured at Höchst under the superintendence of Dr. Pauli, to whose kindness the speaker is indebted for an interesting series of specimens illustrative of the manufacture of antipyrine.

$$\underset{\text{Aceto-acetic ether}}{CH_3.CO.CH_2.CO_2C_2H_5} + \underset{\text{Phenylhydrazine}}{C_6H_5.NH.NH_2}$$

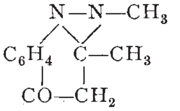
$$= H_2O + C_2H_5.OH + \underset{\text{Pyrazol}}{C_{10}H_{10}N_2O}$$

$$C_{10}H_{10}N_2O + ICH_3 = \underset{\text{Antipyrine-hydriodide}}{IH.C_{10}H_9(CH_3)N_2O.}$$

Dr. Knorr formulates pyrazol thus:



And antipyrine is



The antipyretic effect of this compound is strikingly shown in the following temperature readings in a case of typhoid kindly communicated to the speaker by his friend Dr. Dreschfeld of Manchester. Each of the second set of readings was made two hours after a dose of 30 grains of antipyrine had been administered.

I.	II.	Diff.
°	°	°
105·0	103·0	2·0
103·5	100·2	3·2
103·8	100·8	3·0
105·2	101·4	3·8
104·4	100·6	3·8

Thalline.—The third of the artificial febrifuges is *thalline*, which is offered as the tartrate and sulphate. It is manufactured by the Badische Company. Thalline is said to be used as an antidote for yellow fever. Its scientific name is tetrahydroparaquinanisol, and it was first prepared by Skraup by the action of methyl iodide and potash on paroxyquinoline.

We must, however, bear in mind that none of these synthetical febrifuges are antiperiodics, and therefore cannot be employed instead of the natural alkaloid quinine in cases of ague or intermittent fevers.

Coal-tar Aromatic Perfumes.—A third group of no less interest comprises the artificial aromatic essences, and of these may here be mentioned, in the first place, *cumarin*, $C_9H_6O_2$, the crystalline solid found in the sweet woodruff, in Tonka bean, and in certain sweet-scented grasses. This is now artificially prepared by acting upon sodium salicyl aldehyde with acetic anhydride by the reaction which is associated with the name of Dr. Perkin, and is used in the manufacture of the perfume known as "extract of new-mown hay."

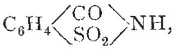
A second interesting case of a production of a naturally occurring flavour is the artificial production of *vanillin*, the crystalline principle of vanilla. Vanilla is the stalk of the *Vanilla planifolia*, which incloses in its tissues prisms of crystalline vanillin, to which substance it owes its fragrance. Tiemann and Harrmann showed that vanillin is the aldehyde of methyl protocatechuic acid—

$$C_6H_3(OH)\,(OCH_3)\,CHO, [CHO : OCH_3 : OH = 1 : 3 : 4].$$

The chief seats of the vanilla productions are on the slopes of the Cordilleras north-west of Vera Cruz in Mexico, also the island of Réunion, and in the Mauritius. Since the discovery of the artificial production of vanillin, the growth of the vanilla has been very much restricted.

A variety of vanilla, termed vanillon, obtained in the East Indies, has long been used in perfumery for preparing "essence of heliotrope." This contains vanillin together with an oil, which is probably oil of bitter almonds. The essence of white heliotrope is now entirely prepared by synthetical operations. It is manufactured by adding a small quantity of artificial oil of bitter almonds to a solution of artificial vanillin; when these substances are allowed to remain for some time in contact, the mixture assumes an odour closely resembling that of natural heliotrope. Through the kindness of Mr. Rimmel the speaker was able to render the fragrance of this coal-tar perfume perceptible to his audience. Nor must we forget to mention the so-called essence of mirbane (nitrobenzene), of which about 150 tons per annum are used for perfuming soap; and artificial oil of bitter almonds, employed as a flavour in place of the natural oil.

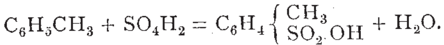
Coal-tar Saccharine.—Of all the marvellous products of the coal-tar industry, the most remarkable is perhaps the production of a sweet principle surpassing sugar in its sweetness *two hundred and twenty* times. This substance is not a sugar, it contains carbon, hydrogen, sulphur, oxygen, and nitrogen. Its formula is



$$C_6H_4 \left\langle \begin{matrix} CO \\ SO_2 \end{matrix} \right\rangle NH,$$

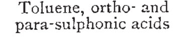
and its chemical name is benzoyl sulphonic imide, or for common use, saccharine. It does not act as a nutriment, but is non-poisonous, and passes out of the body unchanged. The following is a concise statement of its properties, and mode of production from the toluene of coal-tar. It should, however, be first mentioned that the compound benzoyl sulphonic imide (saccharine) was first discovered by Constantin Fahlberg and Remsen, in America. But no patent was taken out for a commercial process till recently, and it is now patented in this country.

STEP I.—Toluene is treated with fuming sulphuric acid in the cold, or it is heated with ordinary sulphuric acid of 168½° Twaddell on the water-bath, or not above 100° C. The latter method is the better. The acid is best caused to act upon the toluene in closed vessels rotating on horizontal axles.

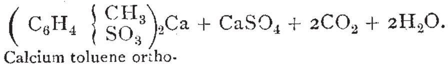


$$\underset{\text{Toluene}}{C_6H_5CH_3} + SO_4H_2 = \underset{\substack{\text{Toluene sulphonic acids}\\ \text{(ortho and para).}}}{C_6H_4\left\{\begin{matrix} CH_3 \\ SO_2.OH \end{matrix}\right.} + H_2O.$$

STEP II.—After all toluene (which as toluene is insoluble in the acid) has disappeared, the contents of the agitating vessel are run into wooden tanks in part filled with cold water, and the whole liquid is stirred up with chalk to neutralise the excess of sulphuric acid used and to obtain the two isomeric toluene sulphonic acids as calcium salts.



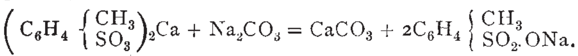
$$2\underset{\substack{\text{Toluene, ortho- and}\\ \text{para-sulphonic acids}}}{\left(C_6H_4\left\{\begin{matrix} CH_3 \\ SO_2OH \end{matrix}\right.\right)} + SO_4H_2 + 2(CaCO_3) =$$



$$\underset{\substack{\text{Calcium toluene ortho-}\\ \text{and para-sulphonates}}}{\left(C_6H_4\left\{\begin{matrix} CH_3 \\ SO_3 \end{matrix}\right.\right)_2Ca} + CaSO_4 + 2CO_2 + 2H_2O.$$

The neutralised mass is filtered through a filter-press to separate therefrom the precipitate of gypsum, which is washed with hot water, and the washings added to the filtrate.

STEP III.—The calcium salts are now treated with carbonate of sodium, to obtain the sodium salts, with precipitation of carbonate of calcium. The precipitate is removed by means of a filter-press from the solution containing the sodium ortho- and parasulphonates.



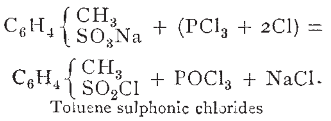
$$\left(C_6H_4\left\{\begin{matrix}CH_3\\SO_3\end{matrix}\right)_2Ca + Na_2CO_3 = CaCO_3 + 2C_6H_4\left\{\begin{matrix}CH_3\\SO_3.ONa.\end{matrix}\right.\right.$$

The sodium toluene sulphonates

STEP IV.—The solution of the sodium salts from III. is evaporated either in an open or in a vacuum-pan so far that a portion taken out will solidify on cooling. The contents of the pan are then run into moulds of wood or iron, and allowed to cool and solidify. The lumps are at length taken from the moulds, broken up small, and dried in a drying-room, and subsequently in a drying apparatus heated with steam, until quite desiccated.

STEP V.—The sodium sulphonate salts are now converted into their corresponding sulphonic chlorides. This is effected as follows:—The dried sulphonates are thoroughly mixed with phosphorus trichloride, itself as dry as possible. The mixture is then placed in lead-lined iron vessels, and a current of chlorine is passed over the mixture till the reaction is ended. The temperature generated by the reaction must be properly regulated by cooling the apparatus with water. The phosphorus oxychloride resulting from the decomposition is driven off, collected, and utilised for developing chlorine from bleaching powder for the chlorinating process, phosphate of lime being precipitated, which can be used in manures. For this purpose the oxychloride is treated with water, and the mixture, now containing hydrochloric and phosphoric acids, is brought into contact with the chloride of lime.

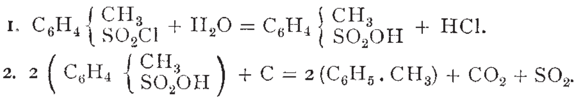
The reaction by which the ortho- and para-toluene sulphonic chlorides are produced is indicated by the following equation:—



$$C_6H_4\left\{\begin{matrix}CH_3\\SO_3Na\end{matrix}\right. + (PCl_3 + 2Cl) =$$
$$C_6H_4\left\{\begin{matrix}CH_3\\SO_2Cl\end{matrix}\right. + POCl_3 + NaCl.$$

Toluene sulphonic chlorides

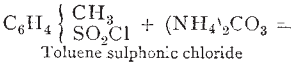
The two sulphonic chlorides remaining in the apparatus are allowed to cool slowly, when the solid one (the para compound) is deposited in large crystals, so that the liquid one can be easily removed by the aid of a centrifugal machine. The crystalline residue is freed from all the liquid sulphonic chloride by washing with cold water. Only the liquid orthotoluene sulphonic chloride is capable of yielding saccharine, and the liquid product above separated is cooled with ice to crystallise out the last traces of the crystalline compound. The solid parasulphonic chloride obtained as by-product, is decomposed into toluene, hydrochloric, and sulphurous acids by mixing it with carbon, moistening the mixture, and subjecting it under pressure to the action of superheated steam. The total change proceeds in two stages:—



$$1.\ C_6H_4\left\{\begin{matrix}CH_3\\SO_2Cl\end{matrix}\right. + H_2O = C_6H_4\left\{\begin{matrix}CH_3\\SO_2OH\end{matrix}\right. + HCl.$$
$$2.\ 2\left(C_6H_4\left\{\begin{matrix}CH_3\\SO_2OH\end{matrix}\right.\right) + C = 2(C_6H_5.CH_3) + CO_2 + SO_2.$$

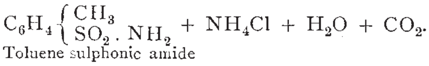
The toluene is then used again in Step I., and the hydrochloric and sulphurous acids in Step VII.

STEP VI.—The liquid orthotoluene sulphonic chloride is now converted into the orthotoluene sulphonic amide by treating the former with solid ammonium carbonate in the required proportions, and subjecting the resulting thick pulpy mixture to the action of steam. Carbonic acid is set free, and a mixture of orthotoluene sulphonic amide and ammonium chloride remains.



$$C_6H_4\left\{\begin{matrix}CH_3\\SO_2Cl\end{matrix}\right. + (NH_4)_2CO_3 =$$

Toluene sulphonic chloride

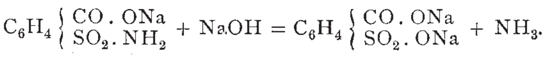


$$C_6H_4\left\{\begin{matrix}CH_3\\SO_2.NH_2\end{matrix}\right. + NH_4Cl + H_2O + CO_2.$$

Toluene sulphonic amide

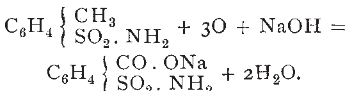
As the mixture is very liable to solidify on cooling, cold water is at once added to prevent this, and to dissolve out the ammonium chloride, the amide remaining in the solid state. The liquid is separated by centrifugating.

STEP VII.—The orthotoluene sulphonic amide is now oxidised, preferably by means of potassium permanganate. The result of this will be, precipitated manganese dioxide, free alkali and alkaline carbonate, and an alkaline ortho sulphamido-benzoate. The alkaline liquid requires careful neutralisation during the oxidising process, and especially before evaporating, with a mineral acid, or else the sulphamido-benzoate formed would be again split up into orthosulphonic benzoate and free ammonia, thus:—



$$C_6H_4\left\{\begin{matrix}CO.ONa\\SO_2.NH_2\end{matrix}\right. + NaOH = C_6H_4\left\{\begin{matrix}CO.ONa\\SO_2.ONa\end{matrix}\right. + NH_3.$$

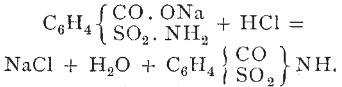
The oxidation process itself is thus represented:—



$$C_6H_4\left\{\begin{matrix}CH_3\\SO_2.NH_2\end{matrix}\right. + 3O + NaOH =$$
$$C_6H_4\left\{\begin{matrix}CO.ONa\\SO_2.NH_2\end{matrix}\right. + 2H_2O.$$

Sodium orthotoluene sulphamido-benzoate

By precipitation with dilute mineral acids, such as hydrochloric or sulphurous acids, the pure benzoyl sulphonic imide is at once precipitated:—



$$C_6H_4\left\{\begin{matrix}CO.ONa\\SO_2.NH_2\end{matrix}\right. + HCl =$$
$$NaCl + H_2O + C_6H_4\left\{\begin{matrix}CO\\SO_2\end{matrix}\right\}NH.$$

"Saccharine," or benzoyl sulphonic imide

Saccharine possesses a far sweeter taste than cane sugar, and has a faint and delicate flavour of bitter almonds. It is said to be 220 times sweeter than cane sugar, and to possess considerable antiseptic properties. On this account, and because of its great sweetness, it is possible that it may be useful in producing fruit preserves or jams, consisting of almost the pure fruit alone; the small percentage of saccharine necessary for sweetening these preserves being probably sufficient to prevent mouldiness. Saccharine has been proved by Stutzer, of Bonn, to be quite uninjurious when administered in considerable doses to dogs, the equivalent as regards sweetness in sugar administered, being comparable to over a pound of sugar each day. Stutzer found, moreover, that saccharine does not nourish as sugar does, but that it passes off in the urine unchanged. It is proposed thus to use it for many medical purposes, where cane sugar is excluded from the diet of certain patients, as in cases of "diabetes mellitus," and in this respect it may prove a great boon to suffering humanity, although we must remember that, as certain of the aromatic compounds if administered for a length of time are known to exert a physiological effect, especially on the liver, it will be desirable to use caution in the regular use of saccharine until its harmless action on the human body has been ascertained beyond doubt.

Saccharine is with difficulty soluble in cold water, from hot aqueous solutions it is easily crystallised. Alcohol and ether easily dissolve it. Hence from a mixture of sugar and saccharine, ether would easily separate the saccharine by solution, leaving the sugar. It melts at about 200° C. with partial decomposition.

The taste is a very pure sweet one, and in comparison with cane sugar it may be said that the sensation of sweetness is much more rapidly communicated to the palate on contact with saccharine than on contact with sugar. The speaker expressed his thanks to the discoverer of saccharine, Dr. Fahlberg, of Leipzig, for a complete and interesting series of preparations illustrating the domestic and medicinal uses of this remarkable compound, and also to his friend Mr. Watson Smith for the kind aid afforded him in the experimental illustration of his discourse.

SOCIETIES AND ACADEMIES

LONDON

Royal Society, May 20.—"On the Working of the Harmonic Analyser at the Meteorological Office." By Robert H. Scott, F.R.S., and Richard H. Curtis, F.R.Met.Soc.

On the 9th of May, 1878, Sir W. Thomson exhibited to the Society a model of an integrating machine, which consisted of a series of five of the disk, globe, and cylinder integrators, which had been devised two years earlier by his brother Prof. James Thomson, and a description of which will be found in the *Proceedings* of the Royal Society, vol. xxiv. p. 262. Sir W. Thomson's paper describing this model will be found in vol. xxvii. of the *Proceedings*, p. 371; and reference should be made to both these papers for an explanation of the principle of the machine. In the communication last named it is stated that the machine was about to be "handed over to the Meteorological Office, to be brought immediately into practical work."

The model was received at the Office in the course of the